Audotory middle-latency fields and potentials: Dependence upon stimulus intensity and stimulus shape

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1 Introduction

Human auditory transient evoked responses are classified according to their peak latencies relative to the eliciting auditory stimulus. The middle latency responses (MLR) occure in the time range from 8 to 50 ms. Six different components have been reported in this time interval: N0 (latency about 8 ms), P0 (12 ms), Na (18 ms), Pa (30 ms), Nb (40 ms) and P1 (or Pb) (50 ms).

The neural generators of the Na/Pa complex are localized in the postero-medial part of the first transverse gyrus (first Heschl's gyrus) by means of MEG source analysis [1, 2, 3, 4] and direct intracerebral recordings from the human auditory cortex [5]. The localization of the subsequent components Nb and P1 is not that clear. However, intracranial recordings yield sources successively located along the gyrus of Heschl.

While many MEG studies deal with the late component N1 less is known about the MLR especially about their dependence on stimulus parameters such as frequency, intensity, rise time and stimulus shape. Therefore, the aim of this study was to investigate the influence of the stimulus intensity and the stimulus shape on the middle latency components Na, Pa, Nb and P1 by means of MEG source analysis.

2 Methods

2.1 Subjects

Seven healthy righthanded volunteers (two female) in the age of 22 to 32 years participated in this study. Their normal auditory status was verified by means of pure tone audiometry. Informal consent was obtained from all subjects after explaining the aim of the study in accordance with the Ethic Comission of the University of Münster and the Declaration of Helsinki. Subjects were paid for their participation.

2.2 Stimulation

Rarefaction clicks and tone pips were delivered to the subject's right ear at a rate of 8 per second. The clicks had a rectangular shape of 1 ms duration. The tone pips had a carrier frequency of 250 Hz and a cosine shaped envelope of 25 ms duration (12.5 ms rise time). The stimuli were presented at intensities of 40, 60 and 80 dB$_{SL}$, respectively ($SL =$ sensation level).

2.3 Data acquisition

Recordings were carried out in a magnetically and acoustically shielded room using a 37 channel neuromagnetometer (MAGNES, Biomagnetic Technologies). The sensor array was placed above the left temporal plane contralateral to the right stimulated ear. Additionally, electric potentials from one electrode placed at C_Z referenced to the left mastoid were recorded. After preamplification (NeuroScan) the EEG signal underwent the same recording and processing procedures as the MEG signal.

The 37 channels of MEG data and the EEG signal were continously recorded (bandwidth 1-200 Hz, sampling rate 520.8 Hz, 16 bit).

Two experimental sessions were carried out for every subject, one for each stimulus type. During the session the stimulus was delivered continuously in runs of 200 s duration at a fixed intensity. Four runs were performed for each of the three different intensities in a randomized order yielding a total of 12 runs. These 12 runs built up one block and two blocks built up one experimental session. The two blocks were separated by a break of 15 min during which the subject was allowed to get up and walk around.

2.4 Data analysis

For each stimulus type one experimental session consisting of two blocks with 12 runs of 200 s duration was available for data analysis. The various runs were broken up into stimulus related epochs of 1 s duration. Since the stimulus was presented continuously for 200 s at a rate of 8 per second, 1600 epochs were available for averaging. Epochs with MEG amplitudes greater than 4 pT and EEG amplitudes greater than 100 μV were considered as artefacts and were rejected. Thereafter, the four runs of one block of the same intensity were cross-averaged leading to a further enhancement of the signal-to-noise ratio.

In addition to the averaging, the signals were detrended and filtered using a high pass of 15 Hz and a low pass of 150 Hz (zero-phase shift Butterworth filter, 12 dB/octave).

Source analysis based on the model of a single **e**quivalent moving **c**urrent **d**ipole (ECD) in a spherically symmetric volume conductor was applied to the magnetic field data. Source coordinates were estimated relatively to the sources of the late cortical component N1. The RMS and dipolemoment amplitudes of every component along with the corresponding latencies were determined for the three different intensities yielding the desired intensity characteristics. The grand average of amplitudes and latencies across blocks was used for further evaluation. Linear regression analysis was applied to the latency-intensity and amplitude-intensity characteristics of the RMS values of each subject. The grand averages of the slope m and of the regression coefficient r^2 were calculated.

One-sided, paired t-test was used for statistical evaluation. Results were considered as significant for $p \leq 0.05$.

3 Results

Typcial waveforms of the simultaneously recorded EEG and MEG responses for one subject are shown in Fig. 1. The EEG timeseries in Fig. 1a clearly exhibits the middle latency components Na, Pa, Nb and P1 for click and pip stimulation, respectively. In the MEG timeseries four peaks coincided with the EEG deflections and were labeled in accordance with the electric waves. The polarity reversal of the magnetic waves between the anterior and posterior channel suggests a dipolar source configuration.

The latency characteristics of RMS and dipolemoment values of the middle latency responses are displayed in Fig. 2a and b, respectively. The response latencies of click evoked MLR were shorter compared to those of the tone-pip evoked MLR. All differences were significant, except the RMS latencies of Nb at 60 dB_{SL} and P1 at 40 dB_{SL} and the dipolemoment latencies of Nb at 80 dB_{sl} and P1 at 40 dB_{SL}. The significant differences were in the range from 2.5 ms (Pa at 60 dB_{SL}) to 7.5 ms (Na at 40 dB_{SL}).

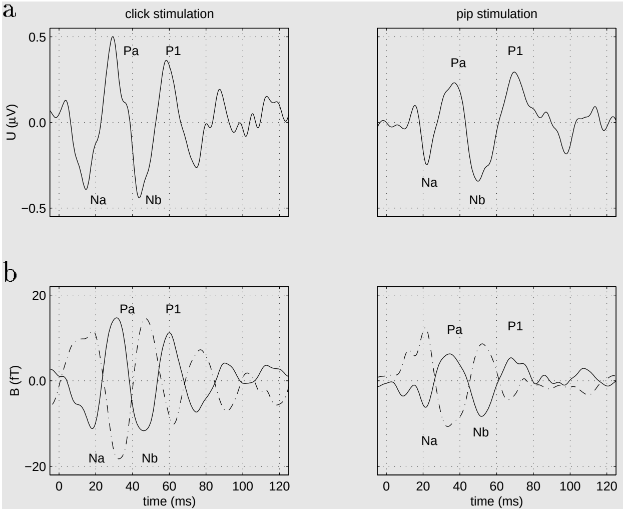

Fig. 1: *a: Electric waveforms of one subject to stimuli at 80 dB* $_{SL}$. *b: Corresponding magnetic waveforms of the maximally responding anterior (solid line) and posterior channel (dashed-dotted line).*

All components became shorter in latency as the stimulus intensity increased. The tone-pip evoked Na wave exhibited the largest latency decrease among all components. Its latency reduced by about 5 ms as intensity changed from 40 to 80 dB_{SL}. Linear regression analysis yielded a slope of -0.11 ms/dB (r^2=0.89), which is significantly different from zero. In contrast, the click evoked Na latency decreased only by about 1 ms in the same intensity range with a small but significant slope of -0.03 ms/dB (r^2=0.81). Pa behaves in almost the same manner. The tone-pip elicited Pa reduced in latency by about 3 ms (-0.08 ms/dB, r^2=0.64) as intensity raised from 40 to 80 dB_{SL}, whereas the click evoked Pa exhibited nearly no latency-change (-0.01 ms/dB, r^2=42, not significant). The latency decrease of the pip evoked Nb of -0.04 ms/dB (r^2=0.46) was close to significance (p=0.06); on the other hand

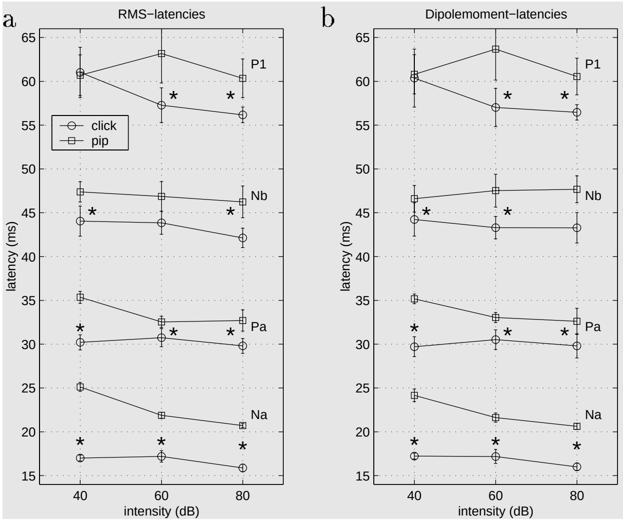

Fig. 2: *Intensity-latency characteristics of the MLR's RMS values (a) and dipolemoments (b) for click and tone-pip stimulation. Each characteristic is labeled by its corresponding component. The errorbars indicate the standard error of the mean. Significant differences are denoted by asterisks.*

no significant results were obtained for the click evoked Nb. The P1 latency shortened significantly by about -0.12 ms/dB (r^2=0.74) in the case of click stimulation. In the case of tone-pip stimulation the slope of -0.04 ms/dB was not significant (p=0.15).

The intensity characteristics of the RMS and dipolemomet amplitudes are displayed in Fig. 3a and b, respectively. Click stimulation tended to evoke somewhat larger response amplitudes for all middle latency waves compared to pip stimulation.

All components exhibited an increase in response amplitude as intensity raised from 40 to 80 dB_{SL}. The characteristics of Na were similar for the tone-pip stimulus (0.04 fT/dB, r^2=0.91) and the click stimulus (0.05 ft/dB, r^2=0.83). Both slopes were significantly different from zero. For Pa only tone-pip stimulation led to a significant slope of 0.09 ft/dB (r^2=0.78), while no intensity effect was obvious for the click elicited Pa. The click evoked Pa began to saturate at 60 dB_{SL}. Similar results were obtained for Nb. No significant amplitude increase was observed in the case of click stimulation, what was due to the saturation at 60 dB_{SL}. Although not significant (p=0.10) in case of tone-

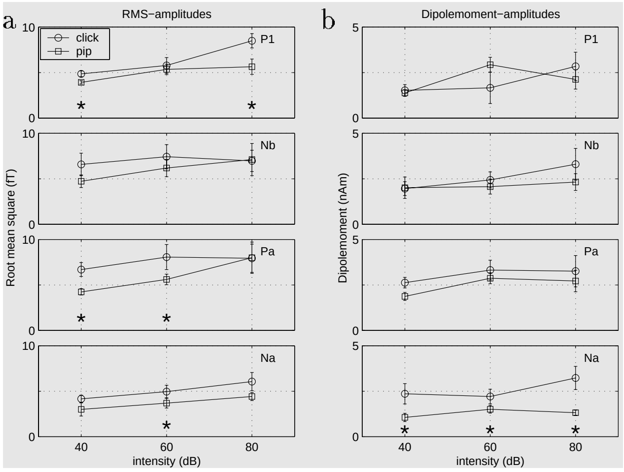

Fig. 3: *Intensity-amplitude characteristics of the MLR's RMS values (a) and dipolemoments (b) for click and tone-pip stimulation. Each characteristic is labeled by its corresponding component. The errorbars indicate the standard error of the mean. Significant differences are denoted by asterisks.*

pip stimulation Nb tended to greater amplitudes with a slope of 0.07 ft/dB (r^2=0.60). The amplitude characteristics of P1 exhibited a significant increase of the RMS amplitude with intensity for both types of stimulation: 0.09 ft/dB, r^2=0.72, $p<0.01$ for click and 0.05 ft/dB, r^2=0.67, $p<0.05$ for tone-pip stimulation.

Dipole source localization yielded the following results: In the posterior-anterior direction all components (except Na after click stimulation) were located more anterior than N1. In the lateral direction the MLR sources were more medial than N1, i.e. they were located deeper in the auditory cortex. No significant differences between MLR and N1 sources could be observed in the inferior-superior direction.

The sources of the middle latency waves were located the more anterior and lateral the later the waves arose. Na, Pa, Nb and P1 were successively situated at more superficial locations for click stimulation, and Pa, Nb and P1 for tone-pip stimulation.

4 Discussion

The shorter latencies of the click evoked responses are in line with the results of Maurizi et al. [6].

They observed an increase of 2 to 4 ms in response latency of the middle latency components as the stimulation was changed from clicks to tone-pips. All components shortened in latency as stimulus intensity increased. This effect was more pronounced for the tone-pip evoked responses.

These latency differences can be interpreted with the threshold model [7]. This model assumes that whenever the acoustic signal reaches a fixed threshold an auditory onset response will be excited. Since an acoustic click reaches its plateau instantaneously the presumed trigger threshold will do so as well independently from stimulus intensity. This might explain the slight intensity effect on response latency during click stimulation as observed for Na and Pa. In contrast the cosine shaped tone pips with a constant rise time of 12.5 ms will reach the threshold earlier as stimulus intensity increases. This results in a stronger dependence on stimulus intensity as observed for Na and Pa. The shorter latencies of click evoked compared to the tone-pip evoked responses can be explained in the same way. Click evoked responses reach their threshold simultaneously to the stimulus onset, whereas the threshold for pip evoked responses is reached somewhat later on the rising edge of the cosine shaped envelope. In the model of Heil [8] the response latency depends on the acceleration of the rising edge (second derivative) of the stimulus envelope. In the case of click stimulation the acceleration is infinity at click onset independent from intensity. Therefore the click evoked response latencies should be scarcely affected by stimulus intensity as predicted by the threshold model. In the case of a cosine shaped envelope the latency intensity-characteristics should not be changed by using Heil's model instead of the threshold model. As already argued by Roß et al. [9] the acceleration of a cosine shaped envelope given by its second derivative has the same shape.

The observed differences in the amplitudes of click and pip evoked responses may be due to the different spectral contents of the stimuli. The click covers a wider spectral range resulting in a larger activation of the basilar membrane. Therefore, more afferent nerve fibers are activated yielding to the larger response amplitudes.

The results of dipole localization confirm those of the studies mentioned in the introduction. The sources are located more anterior and more medial as N1, probably along the Heschl's gyrus.

Acknowlegments

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